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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,360	06/28/2001	Harukazu Fukami	001560-403	2680

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EXAMINER
TRUONG, TAMTHOM NGO

ART UNIT	PAPER NUMBER
1624	13

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/869,360	FUKAMI ET AL.	
	Examin r	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *11-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application is a 371 of PCT/JP 00/07706. Applicant's claim of foreign priority to JP 11-311257 is acknowledged. Claims 1-18 are pending.

1. Applicant's election of species A in paper #11 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Due to the broad scope of the claims, the following restriction is necessary.

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-10 drawn to a chymase inhibitor or compounds of formula I, and pharmaceutical composition thereof, classified in class 544, subclasses 284, 285, etc; also classes 540, 546, 548, 558, 560, and various subclasses.

II. Claims 11-18, drawn to method of treating or preventing a disease accompanied by abnormal vascular function, and method of suppressing lipid deposition in a blood vessel, classified in class 514, subclasses 266.2, 266.3, 266.31, etc.

Inventions groups I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, another compound can treat or prevent a disease of abnormal vascular function (e.g., Calan, Procardia, Tenolol, etc.). Likewise, other compounds can suppress lipid deposition in a blood vessel as well (e.g., Lipitor, Mevacor, etc.). Thus, method

claims 11-18 require an entire different search. References that read on method claims might not be related to chymase inhibitor which is recited in claims 1-10.

3. During a telephone conversation with Ms. Donna Meuth on 3-27-03 a provisional election was made with traverse to prosecute the invention of group I, claims 1-10. Affirmation of this election must be made by applicant in replying to this Office action. Claims 11-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

4. **Incorporated By Reference:** On page 6, the enablement for chymase inhibitors is incorporated by reference to several Japanese patents. The preparation and use of said inhibitors are considered as essential material, which shall not be incorporated by reference.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 2, and 5-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claims 1, 2, and 6 appear to recite a compound. However, the term "comprising" seems to suggest an additional compound or ingredient besides a chymase inhibitor. Thus, it is not clear whether a compound or a composition is claimed.

b. Claims 6, 8, and 9 appear as substantial duplicates because they all recite the same scope of formula I. Note, different intended uses in said claims do not have patentable weight because they do not contribute to structural changes in the compounds of formula (I).

c. Claims 7 and 10 are substantial duplicates because they both recite pharmaceutical composition of the same formula I although claim 10 is a dependent claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. **Scope of Enablement:** Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the **preparation and use** of compounds of formula (I) as a chymase inhibitor, does not reasonably provide enablement for the preparation and use of other compounds as a chymase inhibitors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The quantity of experimentation necessary;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The breadth of the claims;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The specification only shows how to make compounds of formula (I), and how to test them for chymase inhibition. There is no guidance on how to make other compounds, and use them as chymase inhibitors. No starting material and no reaction condition for making other

compounds are disclosed. Instead, applicants rely on several Japanese documents for the enablement of compounds other than those of formula I. Such incorporation by reference is improper as stated above. Thus, with an unpredictable nature of the pharmaceutical art, and limited guidance, one skilled in the art will have to carry out undue experimentation to make and use compounds other than those of formula I. As has been ruled by the court in Genetech Inc. v. Novo Nordisk, failure to disclose any specific starting material or any condition for preparation constitutes lack of enablement, and relying on the knowledge of one skilled in the art cannot cure such deficiency in enablement (**Genetech Inc. v. Novo Nordisk**, 108 F.3d 1361, 42 USPQ 2d 1001 (Fed. Cir. 1997)). Furthermore, the Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the **full scope** of the invention without 'undue experimentation'".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-5 are rejected under 35 U.S.C. **102(a)** as being inherently anticipated by **Ishida et. al.** (WO 99/41277 – cited on IDS). Said reference discloses a chymase inhibitor of formula I which can treat the injury of blood vessel in angioplasty (see the abstract). Although the reference does not relate said compounds to the suppression of lipid deposition, such a property would be inherent in the nature of a chymase inhibitor.

8. Claims 1-10 are rejected under 35 U.S.C. **102(a)** as being anticipated by **Fukami et. al.** (WO 00/ 10982 (cited on IDS)– different inventive entity with common assignee). On page 19, Fukami et. al. discloses a compound [in Example 1], which is embraced by the claimed formula I with the following substituents:

i. A is a phenyl group, and R^1 is hydroxy;

ii. X is a halogen while both R^2 and R^3 are hydrogen.

The disclosed compounds are used to treat a disease with abnormal vascular function (see page 3). Although Fukami does not relate said compounds to the suppression of lipid deposition, such a property would have been inherent by the nature of a chymase inhibitor.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

9. Claims 1-5 are rejected under 35 U.S.C. **102(b)** as being anticipated by **Akaha et. al.** (JP 10-053579 A2 with English abstract and claims). The abstract and claims disclose a chymase inhibitor of formula (I) which can treat and prevent cardiac and circulatory disorders. Thus, the suppression of lipid deposition in a blood vessel is also inherently embraced.

10. Claims 1-5 are rejected under 35 U.S.C. **102(b)** as being anticipated by **Niwata et. al.** (cited on IDS – J. Med. Chem., 1997, 40, pp. 2156-2163). On page 2158, Tables 1 to 3 list several compounds that inhibit chymase. Said compounds can also treat vascular hypertrophy, and other cardiovascular diseases. Thus, it is inherent that they can also treat diseases of abnormal vascular function, and suppress disposition of lipid in a blood vessel.

11. Claims 1-5 are rejected under 35 U.S.C. **102(b)** as being anticipated by the following references:

d. **Akahoshi et. al.** (US 5,948,785 corresponds to WO 96/33974 – cited on IDS): See compounds in Table 1 (columns 83-110), and chymase inhibiting activity on columns 111-112;

e. **Akahoshi et. al.** (US 6,080,738 corresponds to WO 98/18794 – cited on IDS): See compounds in Tables 1 to 9 (columns 37-60), and chymase inhibiting activity on columns 68-70.

Said compounds are used to treat arteriosclerosis. Thus, it is inherent that they can also treat diseases of abnormal vascular function, and suppress disposition of lipid in a blood vessel.

12. Claims 1-5 are rejected under 35 U.S.C. **102(b)** as being anticipated by **Fukami et. al.** (US 5,691,335 correspond to WO 96/04248 – cited on IDS). See compounds in Examples 1-84, and their chymase inhibitory activity in Table 1 (column 27). Said compounds can also treat arteriosclerosis. Thus, it is inherent that they can also treat diseases of abnormal vascular function, and suppress disposition of lipid in a blood vessel.

13. Claims 1-10 are rejected under 35 U.S.C. **102(b)** as being anticipated by **Fukami et. al.** (EP 795,548 – cited on IDS). On page 22 [Example 36], and page 39 [Example 148], Fukami et. al. disclose compounds that are embraced by the claimed formula I with the following substituents:

i. A is phenyl together with R^1 and R^2 form a fused heterocylic system (e.g., quinoline); or

ii. A is phenyl substituted with R^1 as an amino;

iii. X is a halogen, and R^3 is hydrogen;

iv. R^2 is hydrogen when not forming a ring with A and R^1.

The disclosed compounds can inhibit chymase, and treat various circulatory disorders. Again, the reference is silent to the suppression of lipid deposition in a blood vessel; however, such an activity is inherent in the nature of a chymase inhibitor.

14. Claims 1-10 are rejected under 35 U.S.C. **102(e)** as being anticipated by **Fukami et. al.** (US 5,814,631 (cited on IDS) – different inventive entity, but common assignee). On column 29

[Example 36], and column 52 [Example 148], Fukami et. al. disclose chymase inhibitors that are embraced by the claimed formula (I) with the following substituents:

i. A is phenyl together with R^1 and R^2 form a fused heterocylic system (e.g., quinoline); or

ii. A is phenyl substituted with R^1 as an amino;

iii. X is a halogen, and R^3 is hydrogen;

iv. R^2 is hydrogen when not forming a ring with A and R^1.

The disclosed compound can treat disorders of abnormal vascular function as well. Although the reference is silent to the suppression of lipid deposition in a blood vessel, such an activity is inherent in the nature of a chymase inhibitor.

15. Claims 1-5 are rejected under 35 U.S.C. **102(a)** as being anticipated by **Tani et. al.** (WO 00/32587 – US equivalent 6,432,978) On columns 3-5 (of US'978), Tani et. al. disclose several compounds that are chymase inhibitors. On columns 1 and 2, Tani et. al. relate chymase inhibitors to the treatment of various disorders including those of arteriosclerosis, thrombosis, etc. Although Tani et. al. does not associate chymase inhibitors with the suppression of lipid deposition, such an activity is inherently embraced in the treatment of arteriosclerosis – a disease which is often caused by deposition of lipid on the arteriole walls.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Double Patenting

16. The **nonstatutory double patenting** rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 6-10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 8, and 9 of U.S. Patent No. 5,814,631. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant compounds and composition embrace the scope of those claimed in US'631.

18. Claims 6-10 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6, and 20-22 of copending Application No. 09/ 763,213. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant formula I and its composition embrace those claimed in the co-pending application 09/ 763,213.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Information Disclosure Statement

20. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on M-F (9:30-5:00) & every other weekend (fom 3-15).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

T. Truong
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April 2, 2003

RICHARD L. RAYMOND
PRIMARY EXAMINER
ART UNIT 1624